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Research Article

Formulation And Evaluation of Terbinafine Hydrochloride Loaded Solid Lipid Nanoparticle Gel for Topical Delivery

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Abstract
Introduction: Superficial fungal infections such as dermatophytosis remain widespread and are often difficult to treat due to limited drug penetration and systemic side effects of oral antifungals. Terbinafine hydrochloride (TH), although a potent allylamine antifungal, shows poor aqueous solubility and limited skin permeability, reducing its effectiveness in topical formulations.
Objective: To formulate and evaluate a terbinafine hydrochloride-loaded solid lipid nanoparticle (SLN) gel for improved topical delivery, sustained drug release, and enhanced antifungal efficacy.
Methods: TH-loaded SLNs were prepared by hot homogenization followed by ultrasonication using glyceryl monostearate and Poloxamer 407. The optimized SLN (F6) was incorporated into a Carbopol-934 gel base and characterized for particle size, zeta potential, entrapment efficiency, viscosity, pH, spreadability, drug content, in vitro release, antifungal activity, and stability as per ICH guidelines.
Results: The optimized SLN gel (G2) exhibited a particle size of 152.02 nm, zeta potential of -21.8 mV, and entrapment efficiency of 85.52%. It displayed skin-compatible pH (5.46 ± 0.03), uniform drug content (85.47 ± 0.31%), and cumulative drug release of 83.15% over 12 hours, confirming sustained release. Antifungal studies revealed a 17 mm inhibition zone against *Trichophyton rubrum*, comparable to standard miconazole (23 mm). Stability testing over 90 days showed no significant variation in pH, viscosity, or drug diffusion.
Conclusion: The developed terbinafine hydrochloride-loaded SLN gel demonstrated desirable physicochemical stability, controlled drug release, and strong antifungal efficacy, suggesting its potential as a superior and patient-compliant topical therapy for dermatophytosis.

Keywords: Terbinafine hydrochloride, solid lipid nanoparticles, topical gel, antifungal activity, dermatophytosis, sustained release, controlled drug delivery.

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Introduction

Fungal infections of the skin and associated structures represent a significant global health burden, affecting millions of individuals annually. Dermatophytosis is among the most common clinical manifestations, often leading to chronic and recurrent infections that impair quality of life and cause cosmetic and psychological concerns (Gaba et al., 2015; Sharma et al., 2024). Although conventional antifungal agents are widely used, their clinical utility is frequently limited by systemic toxicities such as hepatotoxicity, gastrointestinal disturbances, allergic reactions, and drug–drug interactions (Kumar et al., 2024; Upadhyay et al., 2020). These limitations underscore the need for innovative drug delivery approaches that improve therapeutic efficacy while minimizing systemic exposure.

Terbinafine hydrochloride (TH) is a synthetic allylamine antifungal with potent fungicidal activity against dermatophytes, molds, and certain yeasts. It acts by competitively inhibiting squalene epoxidase, a key enzyme in ergosterol biosynthesis, resulting in intracellular accumulation of squalene and subsequent fungal cell death (Shrestha et al., 2024; Upadhyay et al., 2020). Clinically, TH is available in both oral and topical formulations. Oral administration, while effective, is associated with systemic adverse effects including hepatotoxicity and gastrointestinal disturbances. Conventional topical preparations offer site-specific delivery and reduced systemic toxicity; however, poor aqueous solubility (log P 3.3), limited skin penetration, and short residence time often restrict their therapeutic performance (Begum & Shaik, 2020; Gaba et al., 2015).

Lipid-based nanocarriers, particularly solid lipid nanoparticles (SLNs), have emerged as promising strategies for improving topical delivery of poorly soluble drugs like TH. SLNs consist of biocompatible lipids that solidify at body temperature, encapsulating the drug within a stable lipid matrix. This provides several advantages, including enhanced solubility, protection from chemical degradation, sustained drug release, and improved penetration through the stratum corneum into deeper epidermal and dermal layers (Arabestani et al., 2024; Singh & Verma, 2025; Upadhyay et al., 2020). Compared with conventional gels and creams, SLN-based formulations achieve higher drug deposition at the site of infection, prolong residence time, and reduce systemic absorption.

Recent studies highlight the benefit of incorporating SLNs into hydrogel bases. This combination not only ensures ease of application and improved spreadability but also prolongs retention time at the infection site, promotes uniform drug distribution, and enhances patient compliance (Kesharwani et al., 2016; Shikha et al., 2025). Therefore, development of terbinafine hydrochloride-loaded SLN gels represents an innovative therapeutic approach that integrates the antifungal potency of TH with the delivery advantages of SLN technology, potentially improving treatment outcomes in superficial fungal infections.

Materials and Methods

Materials: Terbinafine hydrochloride (TH) was obtained from Labware Chem. (Nashik, Maharashtra, India). Glyceryl monostearate (GMS) and Poloxamer 407 were purchased from Cosmo Chem. (Pune, India). Tween 80 was procured from Labware Chem. (Pune, India). Carbopol 934 was obtained from Loba Chem. (Mumbai, India), and methyl paraben and propyl paraben were supplied by Moly Chem. (Mumbai, India). All chemicals and solvents were of analytical grade and used without further purification.

Preformulation Studies

Morphological Characterization: The organoleptic properties of terbinafine hydrochloride, including color, odor, taste, and physical nature, were examined as part of the preliminary evaluation (Upadhyay & Mishra, 2020).

Melting Point Determination: The melting point of terbinafine hydrochloride was determined using a capillary tube method. A sealed capillary tube filled with the drug sample was placed in a paraffin-filled melting point apparatus, and the temperature range from initial to complete melting was recorded (Upadhyay et al., 2020).

Solubility Studies: Solubility was assessed by dissolving 50 mg of terbinafine hydrochloride in 3 mL of different solvents (methanol, ethanol, water, phosphate buffer saline pH 7.4). After shaking and centrifugation, the supernatant was analyzed spectrophotometrically for drug solubility (Shikha et al., 2025).

Differential Scanning Calorimetry (DSC): The thermal behavior of terbinafine hydrochloride was analyzed using differential scanning calorimetry (DSC). The presence of a sharp endothermic peak confirmed the crystalline nature and thermal stability of the drug up to its melting point (Gaba et al., 2015).

Ultraviolet–Visible (UV-Vis) Spectroscopy: Standard drug solutions were scanned within the 200–400 nm range using ethanol as blank. The maximum absorbance wavelength (λmax) was determined, and a calibration curve was constructed based on absorbance values at 283 nm (Upadhyay et al., 2020).

Fourier Transform Infrared (FT-IR) Spectroscopy: FT-IR spectra of terbinafine hydrochloride and excipients were recorded in the 4000–400 cm^{-1} range using a PerkinElmer spectrophotometer to investigate possible drug–excipient interactions (Gaba et al., 2015).

Formulation of Terbinafine Hydrochloride–Loaded Solid Lipid Nanoparticles (SLNs)

Seven formulations (F1–F7) of terbinafine hydrochloride-loaded SLNs were prepared by the hot homogenization followed by ultrasonication method (Gaba et al., 2015). The composition of each batch is presented in Table 1.

Table 1. Composition of Terbinafine Hydrochloride–Loaded Solid Lipid Nanoparticles (SLNs)

Batch Code	Active Pharmaceutical Ingredient (API) Quantity in mg	Solid Lipid (mg)	Surfactant (mg)
	Terbinafine hydrochloride	Glyceryl monostearate	Poloxamer 407
F1	50	1000	200
F2	50	1200	200
F3	50	1500	200
F4	50	1000	250
F5	50	1200	250
F6	50	1500	250
F7	50	1000	300

Preparation procedure: Glyceryl monostearate was melted at 70–80 °C, and terbinafine hydrochloride was incorporated into the molten lipid. The aqueous phase was prepared separately by heating surfactant solution (Tween 80 and Poloxamer 407) to the same temperature. The lipid phase was gradually added to the aqueous phase under continuous stirring to form a coarse pre-emulsion. This was further homogenized at 10,000–20,000 rpm for 5–10 minutes using a high-speed homogenizer, followed by ultrasonication for 5–15 minutes to reduce droplet size. The resultant hot nanoemulsion was cooled to room temperature to yield solid lipid nanoparticles (SLNs).

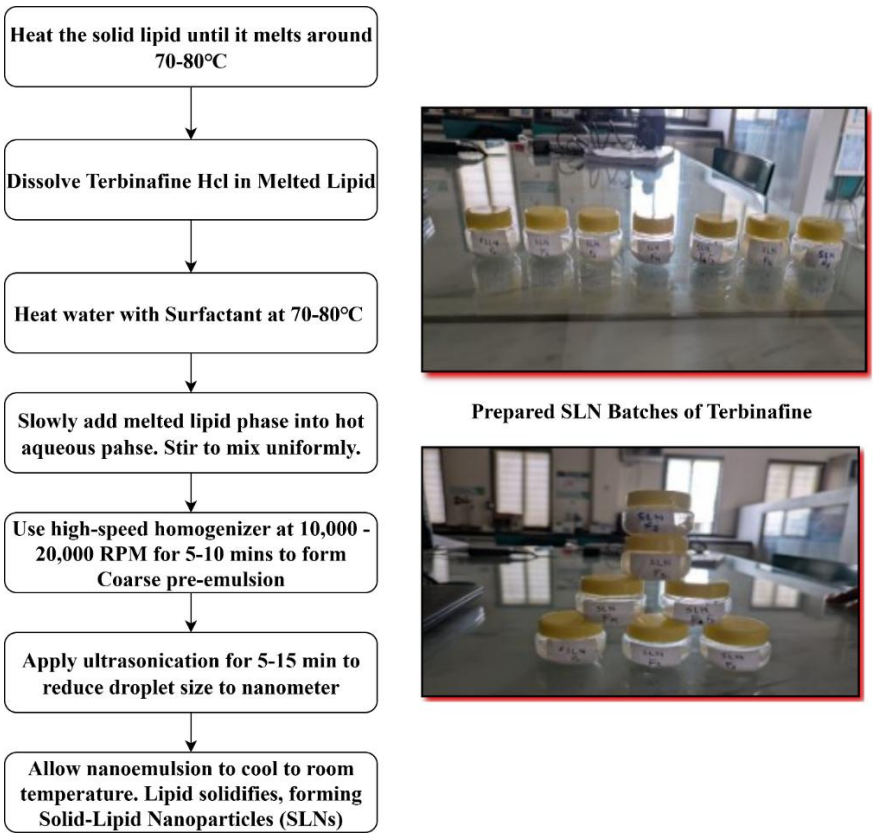


Figure 1. Flowchart for the Preparation of Terbinafine Hydrochloride Loaded Solid Lipid Nanoparticles (SLNs)

Evaluation of SLNs

Entrapment Efficiency: An aliquot (2 mL) of SLN dispersion was centrifuged at high speed, and the supernatant was analyzed spectrophotometrically at 283 nm to determine free drug concentration. Entrapment efficiency (EE) was calculated as:

$$EE\% = \frac{\text{Total drug} - \text{Free drug}}{\text{Total drug}} \times 100$$

Drug Content: SLN dispersions were dissolved in 50% ethanol, diluted with phosphate buffer saline (pH 7.4), and analyzed at 283 nm using a UV

spectrophotometer. Drug content was calculated from the standard calibration curve (Shikha et al., 2025).

In Vitro Drug Diffusion: Diffusion studies were carried out using a Franz diffusion cell fitted with a dialysis membrane (MW cut-off 12,000–14,000 Da). The receptor chamber contained phosphate buffer saline (pH 7.4) maintained at 37 ± 0.5 °C under continuous stirring. SLN-based gels equivalent to 1 mg of drug were placed in the donor compartment. At specified time intervals, 3 mL samples were withdrawn and replaced with fresh buffer. Samples were analyzed spectrophotometrically at 283 nm (Gaba et al., 2015).

Particle Size and Zeta Potential: The mean particle size and polydispersity index were measured using dynamic light scattering (DLS), while the zeta potential was determined by electrophoretic light scattering with a Zetasizer system (Gaba et al., 2015).

Scanning Electron Microscopy (SEM): Surface morphology of the SLNs was examined by SEM at suitable magnifications to confirm particle shape and surface characteristics (Upadhyay et al., 2020).

Stability Studies: Stability studies were performed as per ICH guidelines under different storage conditions: 25 ± 2 °C/60 ± 5% RH and 40 ± 2 °C/75 ± 5% RH for 90 days. Parameters such as physical appearance, pH, entrapment efficiency, and in vitro diffusion were periodically assessed (Shikha et al., 2025).

Formulation of Terbinafine Hydrochloride–Loaded SLN Gel: Optimized SLN dispersion was incorporated into a gel base prepared (Table 2) with Carbopol 934 and HPMC K15M. The polymers were hydrated overnight, followed by the addition of propylene glycol and glycerin. Preservatives (methyl paraben and propyl paraben) were incorporated, and the SLN dispersion was homogenized into the gel at 1000 rpm until uniform consistency was achieved (Upadhyay et al., 2020).

Evaluation of SLN Gel

- **pH measurement:** One gram of gel was dispersed in 100 mL of distilled water and measured with a digital pH meter.
- **Viscosity:** Determined using Brookfield DV-II viscometer with spindle No. 6 at 10 rpm.
- **Spreadability:** Evaluated using the glass slide method, with spreadability (S) calculated as:

$$S = \frac{ML}{T}$$

where M = applied weight, L = slide length, and T = separation time.

Table 2. Composition of Terbinafine Hydrochloride–Loaded SLN Gel Formulations

Parameter	SLNG1	SLNG2	SLNG3
SLN Dispersion (mL)	20	20	20
Carbopol 934 (% w/v)	0.5	1.0	1.5
HPMC K15M (g)	0.5	0.5	0.5
Propylene Glycol (mL)	5	5	5
Glycerin (mL)	5	5	5
Methyl Paraben (g)	0.03	0.03	0.03
Propyl Paraben (g)	0.01	0.01	0.01
Distilled Water (q.s.)	Up to 100 mL	Up to 100 mL	Up to 100 mL

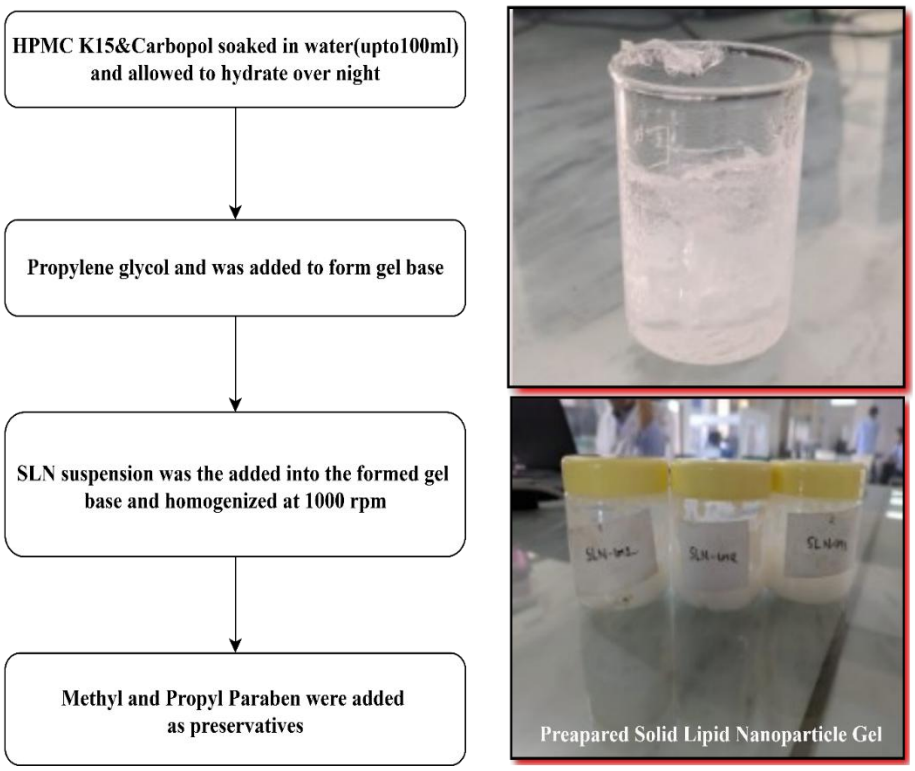


Figure 2. Flowchart for the Formulation of Terbinafine hydrochloride SLN loaded gel

- **Drug content:** Determined by dissolving 1000 mg of gel in ethanol, filtering, and analyzing spectrophotometrically at 283 nm.
- **In vitro diffusion:** Permeation studies were performed using Franz diffusion cells with cellophane membrane in PBS (pH 7.4) at 37 ± 0.5 °C, and samples were analyzed at 283 nm.
- **Antifungal activity:** Evaluated by agar well diffusion method against fungal strains. Zones of inhibition were measured, with miconazole (1 mg/mL) as positive control and DMSO as negative control.
- **Stability testing:** Conducted for 90 days under ICH conditions (25 ± 2 °C/60 ± 5% RH and 40 ± 2 °C/75 ± 5% RH). Gels were monitored for appearance, viscosity, pH, drug content, and in vitro release profile (Shikha et al., 2025).

Results and Discussion

Preformulation Characterization: The pure drug sample of Terbinafine Hydrochloride appeared as a white, odourless, crystalline powder, complying with the Indian Pharmacopoeia (IP) standards (Table 3).

Table 3. Organoleptic Properties of Terbinafine Hydrochloride

Sr. No.	Parameter	IP Specification	Observation
1	Nature	Crystalline	Crystalline
2	Color	Off white	Off white
3	Odour	Odourless	Odourless

Melting Point Determination: The melting point of Terbinafine Hydrochloride was observed in the range of 202–205°C, confirming its purity and compliance with reported literature values.

Solubility Studies: The solubility of Terbinafine Hydrochloride was determined in various solvents, and ethanol was selected as the primary solvent due to its higher solubilizing capacity. UV absorbance was measured at 283 nm (Table 4).

Table 4. Solubility of Terbinafine Hydrochloride

Sr. No.	Solvent System	Solubility
1	Water	Slightly soluble
2	Phosphate buffer (pH 7.4)	Slightly soluble
3	Ethanol	Freely soluble
4	Methanol	Freely soluble

UV Spectrophotometric Analysis and Calibration Curve: The calibration curve of Terbinafine Hydrochloride was developed in ethanol at 283 nm over a concentration range of 5–25 µg/mL. The regression equation was found to be Y = 0.0124x ± 0.045 with a correlation coefficient (R^2) of 0.998, confirming linearity (Table 5 and Figure 3).

Table 5. Absorbance Data of Terbinafine Hydrochloride in Ethanol

Sr. No.	Concentration (µg/mL)	Absorbance (283 nm)
1	5	0.106
2	10	0.168
3	15	0.238
4	20	0.290
5	25	0.356

Calibration Parameters
λmax: 283 nm
Regression equation: Y = 0.0124x ± 0.045
Correlation coefficient (R^2):0.998

The results confirmed that Beer–Lambert's law was obeyed within the specified concentration range.

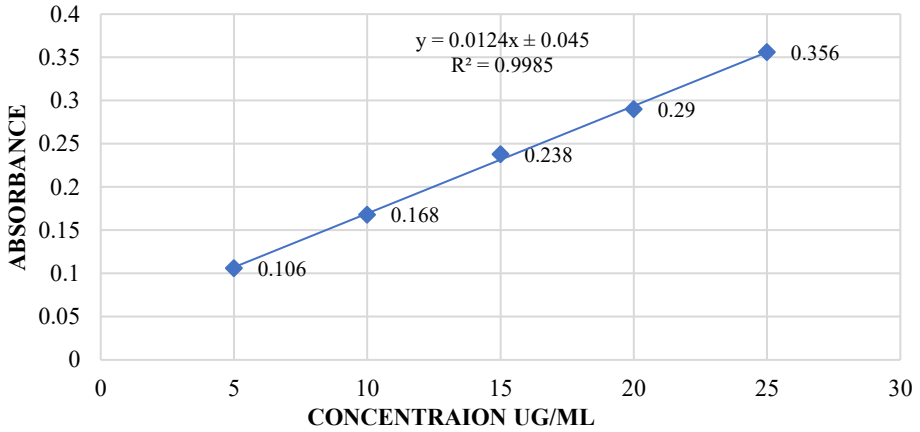


Figure 03: calibration curve of terbinafine hydrochloride

Drug-Excipient Compatibility Studies

The compatibility between Terbinafine Hydrochloride and the selected excipients used in the formulation of solid lipid nanoparticles (SLNs) was evaluated using Fourier Transform Infrared (FTIR) spectroscopy. The spectra of pure drug, individual excipients, their physical mixture, and the optimized SLN gel formulation (G2) were compared to identify any potential chemical interactions.

The FTIR spectrum of Terbinafine Hydrochloride exhibited distinct characteristic absorption bands corresponding to its functional groups O-H stretching at 3674.80 cm^{-1}, C-O stretching at 1004.79 cm^{-1}, and C-Cl stretching at 463.14 cm^{-1}, confirming its structural identity. The physical mixture of drug and excipients showed all the major peaks of the pure drug, with negligible shifts in wavenumber (e.g., O-H at 3306.80 cm^{-1}, C-O at 1009.74 cm^{-1}), indicating no chemical interaction between the drug and excipients. Similarly, the optimized SLN gel (G2) formulation displayed characteristic peaks at 3306.80 cm^{-1} (O–H stretching), 2980.33 cm^{-1} (C-H stretching), and 1042.74 cm^{-1} (C-O stretching), which correspond well with those of the pure drug (Table 6 and Figure 4).

The slight shifts observed in some bands, particularly in the O-H and C-O regions, may be attributed to hydrogen bonding or physical encapsulation of the drug within the lipid matrix rather than any chemical modification. Importantly, there was no disappearance of characteristic peaks or emergence of new peaks in the spectra of the physical mixture and SLN gel, confirming that the molecular structure of Terbinafine Hydrochloride remained intact throughout the formulation process.

Table 6. Comparative FTIR Interpretation of Terbinafine Hydrochloride, API-Excipient Mixture, and Optimized SLN Gel (G2)

Sr. No.	Functional Group	Standard Range (cm^{-1})	API	API + Excipients	SLN Gel G2)	Interpretation (Summary)
1	O-H stretch	3200–3700	3674.80	-	3306.80	Broad O-H retained; slight shift due to H-bonding, no interaction.
2	C-H stretch	2850–2960	-	2879.85	2980.33	Minor shift; aliphatic structure preserved.
3	C-H bend	1300–1470	-	1341.96	-	Bending band unchanged; stable structure.
4	C=C stretch / bend	1600–1680 / 675–900	-	841.64	1642.40 / 901.50	Aromatic C=C bands intact; conjugation unaltered.
5	C-O stretch	1000–1300	1004.79	1009.74	1042.74	Slight shift; encapsulation effect only.
6	C-Cl stretch	500–800	463.14	668.24	-	Halide band retained; no degradation.
7	C-C bend	1400–1600	-	-	1414.06	Confirms intact carbon skeleton.
8	M-O stretch	400–600	-	463.49	-	Lipid/surfactant band; no drug interaction.

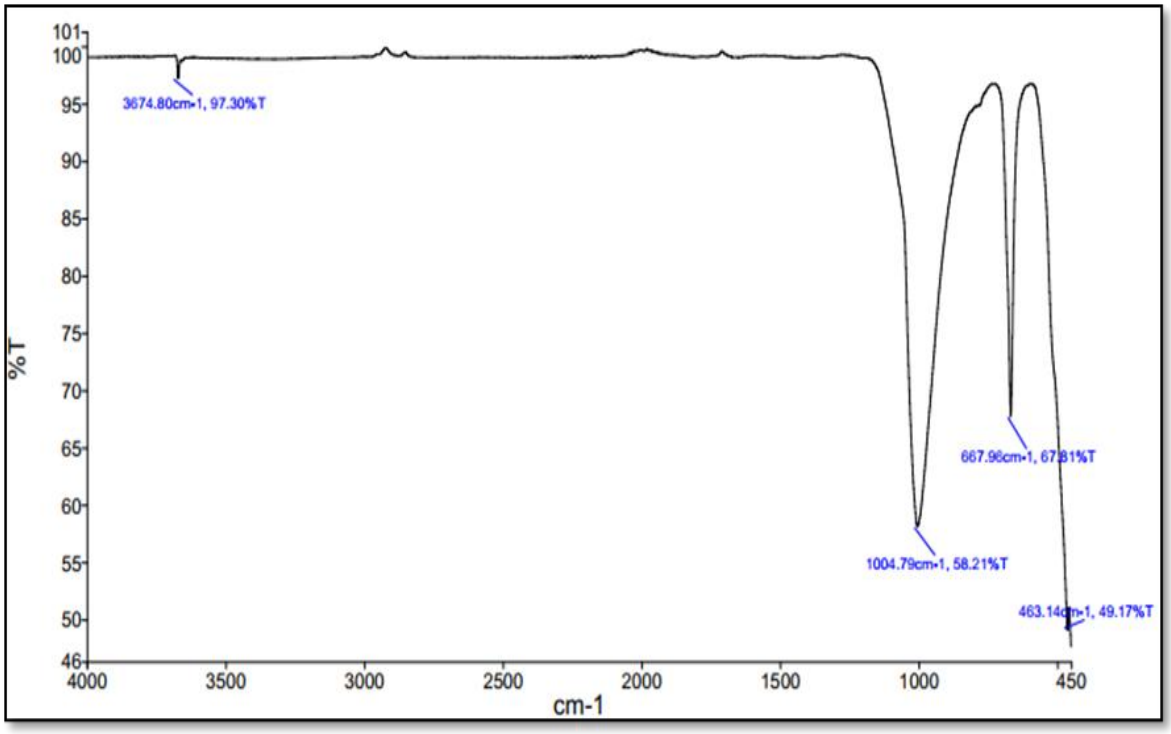


Figure 04a. FTIR spectra of Terbinafine hydrochloride

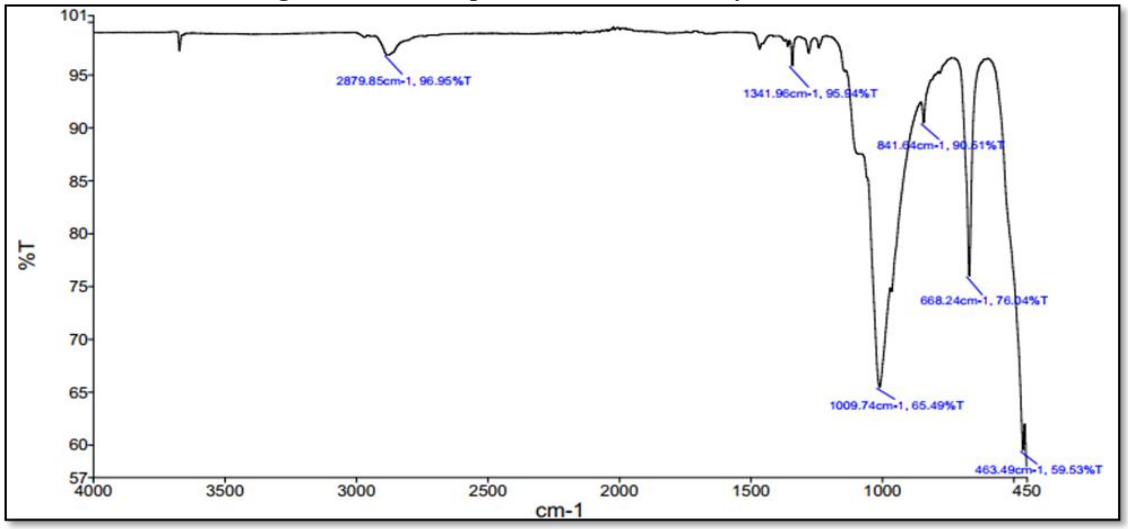


Figure 04b. FTIR Spectra of API + Excipients

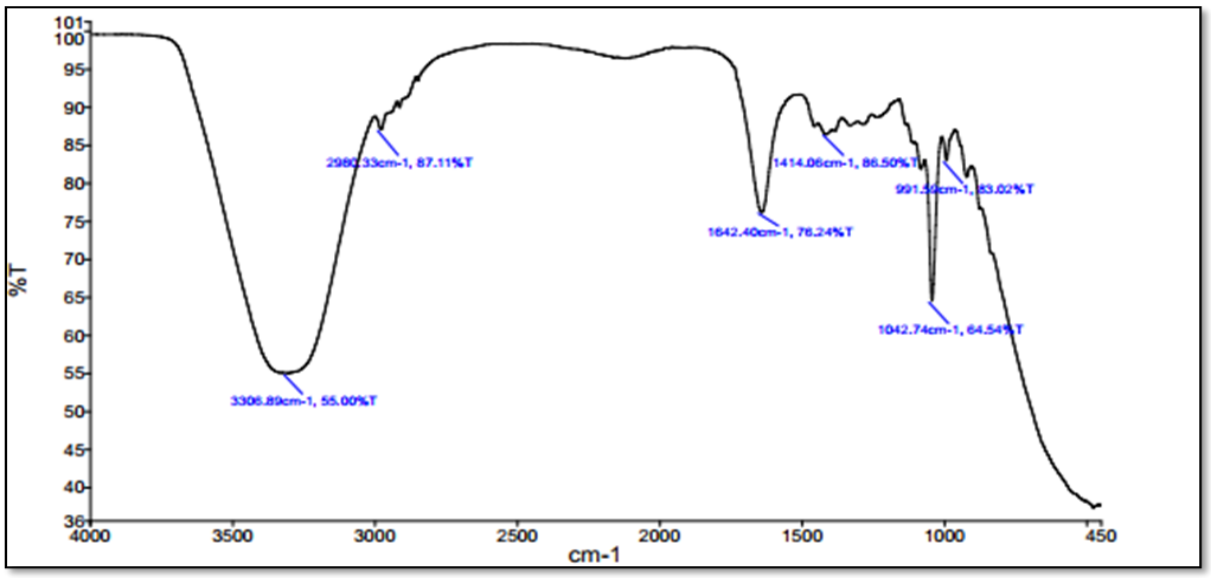


Figure 04c. FTIR Spectra of Optimized SLN Gel (G2)

Differential Scanning Calorimetry (DSC): The DSC thermogram of Terbinafine Hydrochloride exhibited a sharp endothermic peak at 146.52°C, corresponding to its melting point, confirming its crystalline nature and purity. The absence of additional peaks suggested no polymorphic transitions or impurities, validating the drug's stability during formulation.

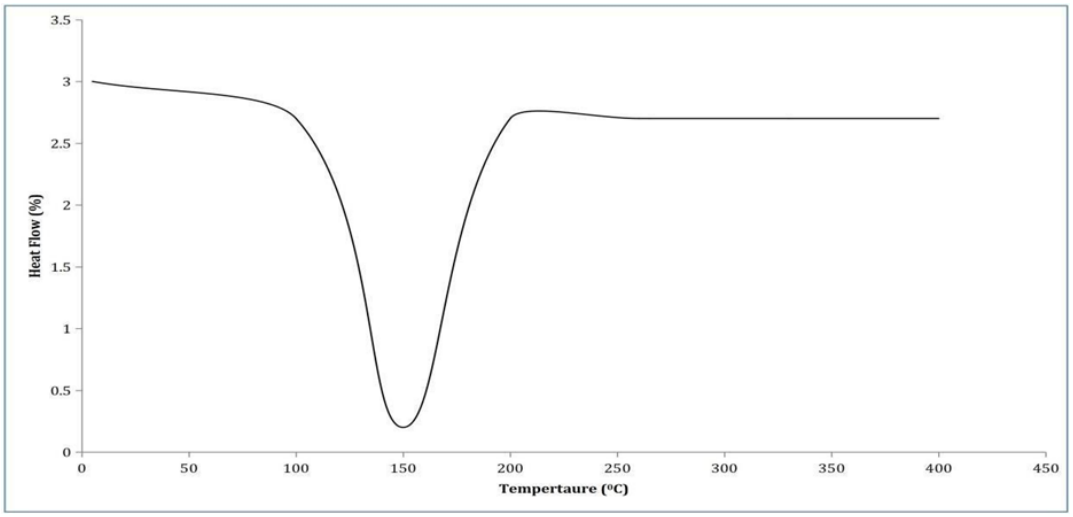


Figure 05: DSC Thermogram of Terbinafine Hydrochloride

Characterization of Solid Lipid Nanoparticles (SLNs)

Appearance: All SLN batches appeared as uniform off-white dispersions, indicating successful nanoparticle formation.

Evaluation of pH, Drug Content, and Entrapment Efficiency: All formulations exhibited pH values within the skin-compatible range (5.14 ± 0.03 to 5.95 ± 0.02), ensuring suitability for topical application. Drug content and entrapment efficiency were satisfactory across batches, with formulation F6 showing the highest drug content (84.64 ± 0.31%) and entrapment efficiency (85.52 ± 0.18%), indicating optimal formulation performance and uniform drug distribution within the SLN matrix (Table 7 and Figure 6).

In Vitro Drug Diffusion Studies: In vitro release profiles revealed sustained drug release up to 12 hours. Among all batches, F6 exhibited the highest cumulative release (83.25 ± 0.11%), indicating effective diffusion and controlled release properties of the SLN formulation (Table 8 and Figure 7).

Particle Size and Zeta Potential: The particle size of the optimized batch (F6) was 152.02 nm with a polydispersity index (PDI) of 0.358, signifying a narrow size distribution suitable for topical delivery. The zeta potential was –21.8 mV, indicating good electrostatic stability and reduced aggregation tendency (Figure 08).

Zeta Potential: The stability of nanoparticle is determined from the zeta potential of optimized batch is within the range, the batch show good stability zeta potential of -21.8 mV (Figure 09).

Table 7. Physicochemical Evaluation of Terbinafine Hydrochloride Solid Lipid Nanoparticle (SLN) Formulations (Mean ± SD)

Formulation Code	pH	Drug Content (%)	Entrapment Efficiency (%)
F1	5.14 ± 0.03	72.69 ± 0.42	74.37 ± 0.27
F2	5.34 ± 0.03	70.97 ± 0.19	75.86 ± 0.22
F3	5.51 ± 0.02	70.16 ± 0.15	72.56 ± 0.35
F4	5.69 ± 0.03	75.51 ± 0.27	76.39 ± 0.29
F5	5.95 ± 0.02	74.64 ± 0.29	78.88 ± 0.22
F6	5.46 ± 0.03	84.64 ± 0.31	85.52 ± 0.18
F7	5.39 ± 0.03	80.56 ± 0.36	81.16 ± 0.20

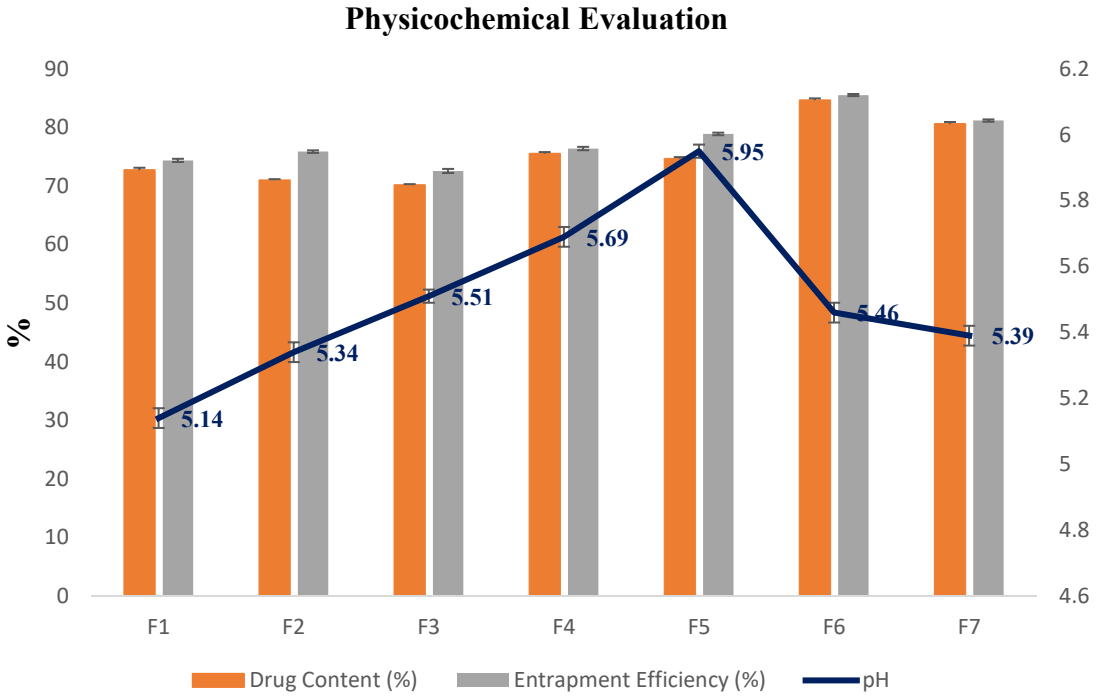


Figure 06. Comparative evaluation of (a) pH, (b) drug content, and (c) entrapment efficiency of Terbinafine Hydrochloride-loaded SLN formulations (F1–F7).

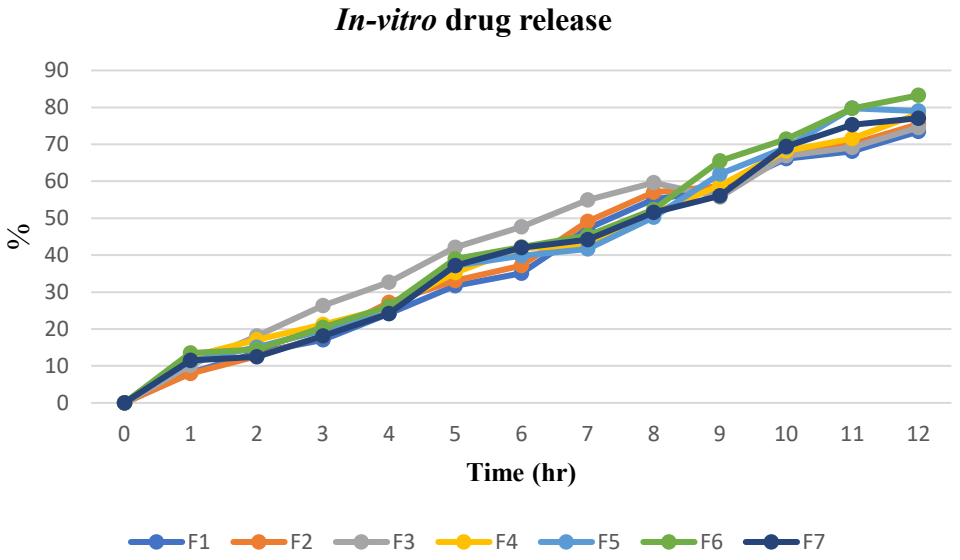


Figure 07. In vitro drug release of TBF HCL loaded SLN (F1-F7) batches

Table No 8. In vitro drug release of TBF HCL loaded SLN(F1-F7) batches

Time (hr)	F1	F2	F3	F4	F5	F6	F7
0	0	0	0	0	0	0	0
1	8.12 ± 0.14	7.92 ± 0.17	10.14 ± 0.13	12.57 ± 0.11	11.34 ± 0.08	13.54 ± 0.10	11.52 ± 0.10
2	13.56 ± 0.04	12.66 ± 0.05	18.06 ± 0.15	17.06 ± 0.08	15.04 ± 0.07	14.48 ± 0.09	12.48 ± 0.09
3	17.09 ± 0.04	18.12 ± 0.14	26.32 ± 0.03	21.23 ± 0.13	19.66 ± 0.11	20.42 ± 0.10	18.06 ± 0.11
4	24.15 ± 0.05	27.22 ± 0.12	32.68 ± 0.08	25.78 ± 0.11	24.27 ± 0.12	26.12 ± 0.08	24.18 ± 0.12
5	31.66 ± 0.17	33.06 ± 0.05	42.06 ± 0.13	35.21 ± 0.10	37.19 ± 0.08	39.02 ± 0.12	37.15 ± 0.11
6	35.08 ± 0.05	37.17 ± 0.10	47.66 ± 0.07	41.92 ± 0.08	39.82 ± 0.12	42.17 ± 0.10	42.02 ± 0.10
7	47.24 ± 0.14	49.12 ± 0.11	54.92 ± 0.16	42.47 ± 0.13	41.63 ± 0.09	45.29 ± 0.11	44.17 ± 0.12
8	55.08 ± 0.13	57.02 ± 0.11	59.63 ± 0.06	51.38 ± 0.11	50.27 ± 0.14	52.36 ± 0.15	51.58 ± 0.13
9	57.73 ± 0.18	58.62 ± 0.11	55.74 ± 0.18	58.81 ± 0.17	61.92 ± 0.15	65.47 ± 0.14	56.06 ± 0.14
10	66.12 ± 0.18	68.32 ± 0.10	66.92 ± 0.05	68.21 ± 0.16	69.17 ± 0.14	71.36 ± 0.16	69.38 ± 0.15
11	68.06 ± 0.17	70.12 ± 0.08	69.15 ± 0.12	71.54 ± 0.15	79.75 ± 0.12	79.67 ± 0.13	75.26 ± 0.14
12	73.45 ± 0.07	75.45 ± 0.15	74.54 ± 0.18	78.25 ± 0.13	79.02 ± 0.12	83.25 ± 0.11	77.06 ± 0.12

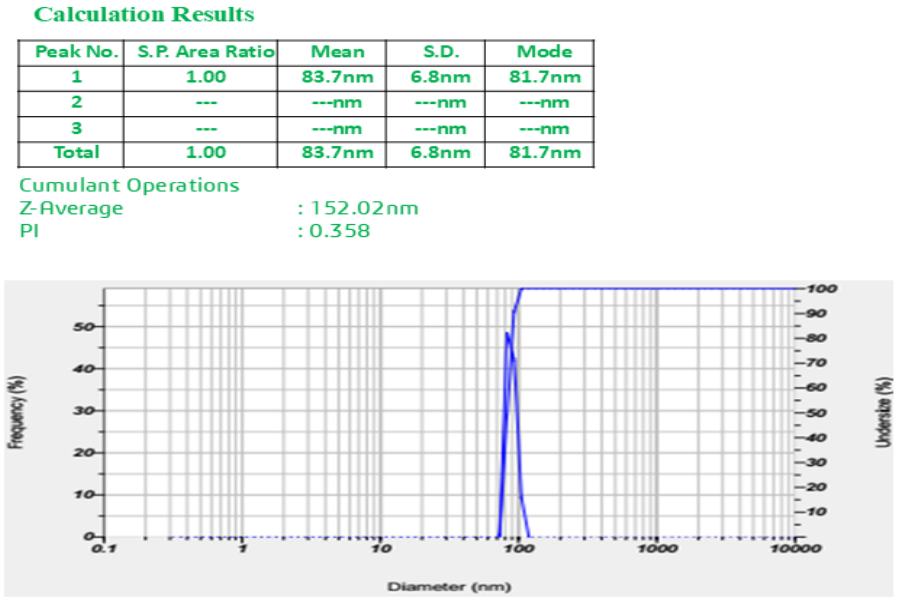


Figure 08. Particle size of optimized batch of SLN (F6)

Calculation Results

Peak No.	Zeta Potential	Electrophoretic Mobility
1	-21.8mV	-0.000227cm2/Vs
2	---mV	--- cm2/Vs
3	---mV	--- cm2/Vs

Zeta Potential (Mean) : -21.8mV

Electrophoretic Mobility Mean : -0.000227cm2/Vs

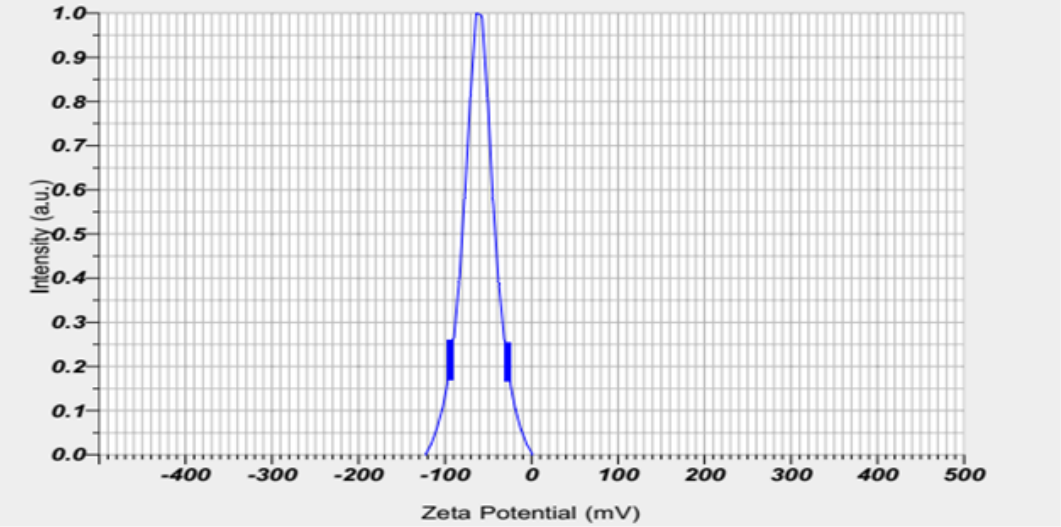


Figure 09. Zeta Potential of optimized batch of SLN (F6)

Scanning Electron Microscopy (SEM): SEM images of the optimized batch (F6) showed spherical nanoparticles with slightly irregular surfaces, characteristic of SLNs prepared with glyceryl monostearate. The morphology confirmed successful nanoparticle formation and uniform size distribution (Figure 10).

Stability Studies of SLNs: Stability studies conducted for 90 days under ICH conditions demonstrated no significant changes in physical appearance, pH, or drug release. The formulation remained physically and chemically stable, confirming formulation robustness (Table 9).

Evaluation of Terbinafine Hydrochloride Loaded SLN Gel

Appearance and Consistency: All gel formulations (G1–G3) appeared off-white, smooth, and uniform without grittiness.

pH: The pH values (5.3–5.4) were within the physiological range of the skin, confirming their suitability for topical application.

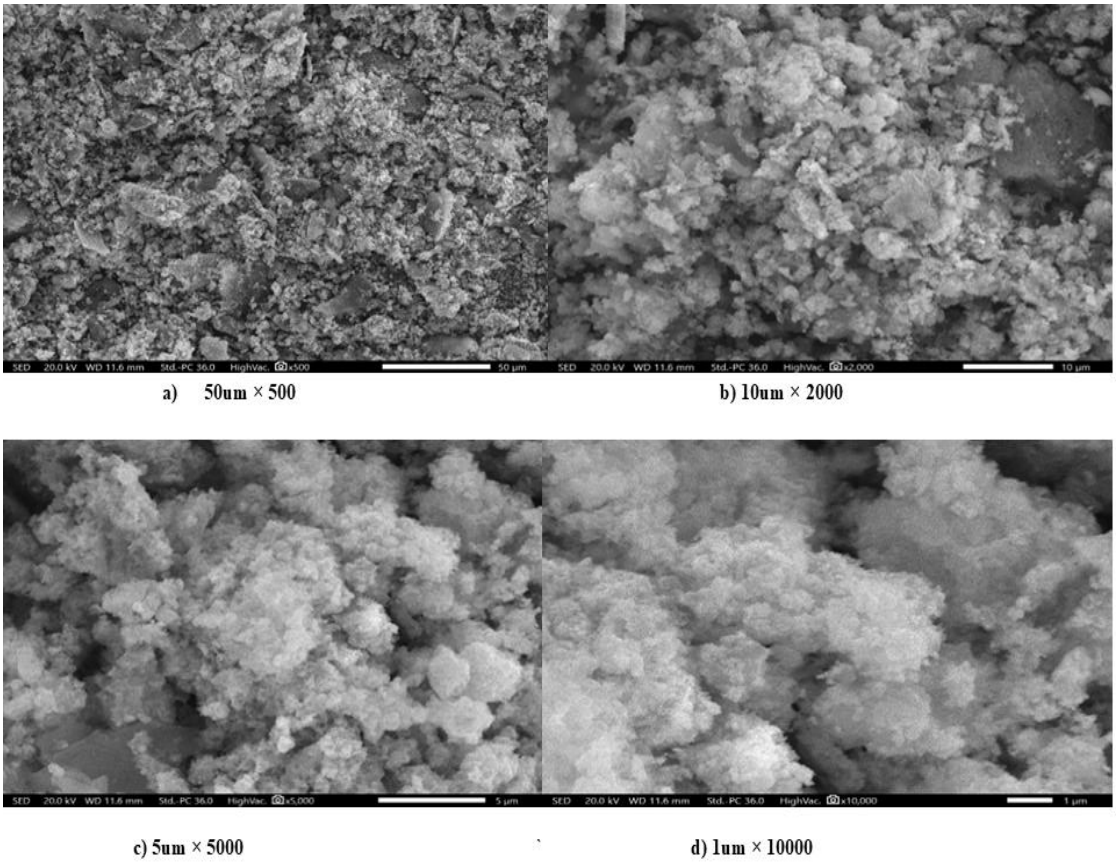
Spreadability and Viscosity: The spreadability of the gels ranged between 7.5–9.6 g·cm/s**,** and viscosity between 6670–8530 cps, indicating desirable consistency and ease of application. The G2 formulation exhibited the best rheological properties.

Drug Content: The drug content ranged from 79.43% to 85.47%**,** with G2 showing the highest drug content (85.47 ± 0.31%), confirming uniform drug distribution.

In Vitro Drug Diffusion: The G2 gel exhibited the maximum cumulative drug release (83.15 ± 0.13% at 12 hours) compared to G1 and G3, indicating improved drug release kinetics due to optimized lipid matrix and gel network.

Antifungal Activity: The antifungal activity of the optimized SLN G2 gel was assessed against *Trichophyton rubrum* (ATCC 53171) using the agar well diffusion method. The G2 formulation exhibited a zone of inhibition of 17 mm**,** comparable to the standard Miconazole (23 mm), demonstrating significant antifungal efficacy

Stability Studies of Optimized SLN Gel (G2): The optimized SLN gel (G2) remained stable over 90 days under both room and accelerated conditions, with negligible changes in appearance, pH, viscosity, and drug release. These results confirm the physical stability and suitability of the developed SLN gel for long-term storage and topical therapeutic use.



a) 50um × 500 b) 10um × 2000

c) 5um × 5000 d) 1um × 10000

Figure 10. SEM images of optimized SLN (F6)

Table No 9. Stability study on optimized SLN formulation

Month	Appearance	pH	In vitro drug diffusion study %	
			25°C/60±5%RH	40°C/75±5%RH
Initial	off white	5.4 ± 0.03	83.35 ± 0.11	83.32 ± 0.08
After 30 days	off white	5.4 ± 0.03	83.05 ± 0.12	82.92 ± 0.10
After 60 days	off white	5.3 ± 0.02	82.49 ± 0.14	82.28 ± 0.11
After 90 days	Off white	5.2 ± 0.02	82.24 ± 0.15	82.15 ± 0.13

Table No 10. Evaluation of Terbinafine Hydrochloride–Loaded Solid Lipid Nanoparticle (SLN) Gels

Parameter	Observation / Results	Remarks / Interpretation
Appearance & Consistency	All formulations (G1–G3) appeared off-white, smooth, uniform, and non-gritty.	Indicates good homogeneity and acceptable physical appearance for topical application.
pH	G1: 5.38 ± 0.03 G2: 5.49 ± 0.04 G3: 5.32 ± 0.02	All formulations showed skin-compatible pH (5.3–5.4), suitable for topical use without irritation.
Spreadability (g·cm/s)	G1: 7.5 ± 0.25 G2: 9.6 ± 0.30 G3: 8.2 ± 0.20	Spreadability inversely related to viscosity; G2 exhibited best spreadability and handling properties.
Viscosity (cps)	G1: 8250 ± 71.61 G2: 8530 ± 40.00 G3: 8480 ± 50.09	Viscosity within 6670–8530 cps range; G2 displayed optimum gel consistency and stability (++).
Drug Content (%)	G1: 81.63 ± 0.35 G2: 85.47 ± 0.31 G3: 79.43 ± 0.33	Uniform drug distribution; G2 showed highest content, confirming efficient drug loading.
In Vitro Drug Diffusion (% at 12 h)	G1: 78.32 ± 0.07 G2: 83.15 ± 0.13 G3: 80.49 ± 0.16	G2 exhibited maximum cumulative release (83.15%), indicating optimized lipid matrix and gel network.
Antifungal Activity (Zone of Inhibition, mm)	Control: 0 Standard (Miconazole): 23 G2 (SLN Gel): 17	G2 showed significant antifungal activity against *Trichophyton rubrum*, comparable to standard drug.
Stability (G2 formulation)	pH 5.1–5.4; Viscosity 8530 → 8875 cps; Drug diffusion ≈ 82%; Appearance: off-white (stable after 90 days at 25°C/40°C)	No significant changes observed after 90 days; formulation remained stable per ICH guidelines.

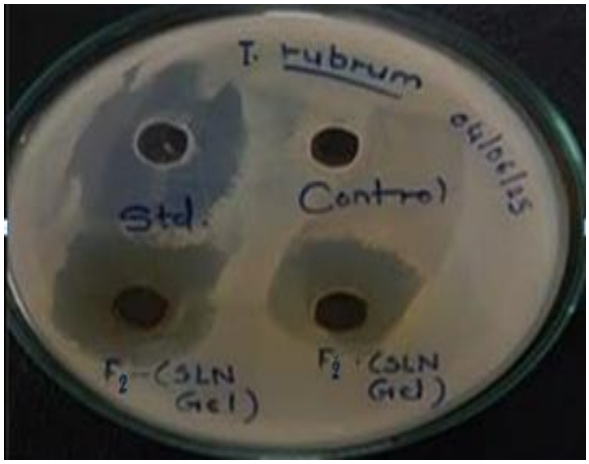


Figure 19: Antifungal study of optimized SLN gel batch (SLN G2)

Conclusion

The present study successfully developed and evaluated a terbinafine hydrochloride–loaded solid lipid nanoparticle (SLN) gel aimed at enhancing the topical delivery and antifungal performance of terbinafine hydrochloride. The optimized formulation (F6-based SLN incorporated as G2 gel) demonstrated ideal physicochemical characteristics, including nanosized particles (152.02 nm), acceptable zeta potential (-21.8 mV), and high entrapment efficiency (85.52%). The gel exhibited skin-compatible pH (5.3-5.5), superior spreadability, and high drug content (85.47 ± 0.31%). In vitro diffusion studies confirmed sustained drug release up to 12 hours, while antifungal testing against Trichophyton rubrum showed strong inhibitory activity comparable to miconazole. Stability analysis under ICH conditions revealed no significant physicochemical changes over 90 days, indicating good formulation robustness.

Overall, the terbinafine hydrochloride-loaded SLN gel offers an improved, stable, and patient-friendly alternative to conventional topical antifungal preparations, enhancing therapeutic efficacy, skin retention, and treatment compliance in dermatophytosis management.

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